

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (CURRENTLY AMENDED) A method for administering an active principle via inhalation by the pulmonary route to a patient, comprising:

providing a biocompatible microparticle, consisting of (a) a core consisting of said active principle, and (b) an external layer of at least one coating agent deposited on said core by a supercritical fluid technique, comprising the optional use of an organic solvent, wherein supercritical fluid is carbon dioxide and the optional organic solvent is present in an amount between 3.5% to 25% by weight relative to the mass of supercritical fluid, ~~wherein said microparticle has a mean diameter of between 1 μ m and 30 μ m and an apparent density of between 0.02 g/cm³ and 0.8 g/cm³; and~~

administering the biocompatible microparticle to said patient in the form of an inhalation aerosol,

wherein said biocompatible microparticle has the following characteristics:

-a mean diameter of between 1 and 15 μ m,

-an apparent density of between 0.02 g/cm³ and 0.8g/cm³,

-an active principle/coating agent mass ratio of between 95/5 and 80/20,

-an external layer comprising a residual quantity of organic solvent of less than 500 ppm, when an organic solvent is added to supercritical fluid.

2. (CURRENTLY AMENDED) The method of claim 1, wherein the microparticle has a mean diameter of between ~~1 μm and 15 μm~~ , and an apparent density of between 0.05 g/cm³ and 0.4 g/cm³.

3. (PREVIOUSLY PRESENTED) The method of claim 1, wherein the microparticle is obtained by a method comprising:

- suspending an active principle in a solution of at least one substantially polar coating agent in an organic solvent, wherein said active principle is insoluble in the organic solvent, said substantially polar coating agent is insoluble in a fluid in a supercritical state, and said organic solvent is soluble in a fluid in a supercritical state,
- bringing the suspension into contact with a fluid in a supercritical state, so as to desolvate in a controlled way the substantially polar coating agent and ensure its coacervation,
- substantially extracting the solvent using a fluid in a supercritical state and discharging the supercritical fluid/solvent mixture, and
- recovering the microparticles.

4. (PREVIOUSLY PRESENTED) The method of claim 1, wherein the microparticle is obtained by a method comprising:

suspending an active principle in a supercritical fluid containing at least one coating agent dissolved therein, and then in ensuring coacervation of the particles by physicochemical modification of the environment.

5. (PREVIOUSLY PRESENTED) The method of claim 3, wherein the coating agent is chosen from:

- biodegradable (co)polymers of α -hydroxycarboxylic acids,
- amphiphilic block polymers of a poly(lactic acid)-poly(ethylene oxide) type,
- biocompatible polymers of a poly(ethylene glycol), poly(ethylene oxide) type,
- polyanhydrides, poly(ortho esters), poly- ϵ -caprolactones, and derivatives thereof,
- poly(β -hydroxybutyrate), poly(hydroxyvalerate), and poly(β -hydroxybutyrate-hydroxyvalerate) copolymers,
- poly(malic acid),
- polyphosphazenes,
- block copolymers of a poly(ethylene oxide)-poly(propylene oxide) type,
- poly(amino acids),
- polysaccharides,
- phospholipids,
- fatty acid esters, and
- mixtures of the abovementioned compounds.

6. (PREVIOUSLY PRESENTED) The method of claim 4, wherein the coating agent is chosen from:

- phospholipids,

- mono-, di-, and triglycerides in which the fatty acid chains range from C4 to C22, and mixtures thereof,

- mixtures of glycerides and of esters of polyethylene glycol,
- cholesterol,
- fatty acid esters,
- biodegradable or bioerodible polymers soluble in a supercritical fluid, and
- mixtures thereof.

7. (PREVIOUSLY PRESENTED) The method of claim 1, wherein the active principle is chosen from proteins, peptides, polysaccharides, anti-asthmatic agents, beta-estradiol hormones, testosterone, bronchodilators, cytotoxic agents, corticoids, antigens, and DNA fragments.

8. (CURRENTLY AMENDED) The method of claim 2, wherein the microparticle is an immediate-release microparticle, ~~and wherein the active principle/coating agent mass ratio of this particle is between 95/5 and 80/20.~~

9-10. (CANCELLED).

11. (PREVIOUSLY PRESENTED) The method of claim 1, wherein the microparticle is obtained according to a method comprising:

- bringing together a coating agent and an active principle; and
- introducing a supercritical fluid, with stirring, in a closed reactor.

12. (PREVIOUSLY PRESENTED) The method of claim 2, wherein the microparticle has a mean diameter of between 2 μm and 10 μm .

13. (PREVIOUSLY PRESENTED) The method of claim 7, wherein the protein or peptide is chosen from insulin, calcitonin, and analogues of luteinizing hormone-releasing hormone.

14. (PREVIOUSLY PRESENTED) The method of claim 7, wherein the polysaccharide is heparin.

15. (PREVIOUSLY PRESENTED) The method of claim 7, wherein the anti-asthmatic agents are chosen from budesonide, beclometasone dipropionate, and beclometasone 17-monopropionate.

16. (PREVIOUSLY PRESENTED) The method of claim 7, wherein the bronchodilator is albuterol.

17. (PREVIOUSLY PRESENTED) The method of claim 5, wherein the biodegradable (co)polymers of α -hydroxycarboxylic acids are selected from homopolymers and copolymers of lactic acid and glycolic acid.

18. (PREVIOUSLY PRESENTED) The method of claim 17, wherein the biodegradable (co)polymers of α -hydroxycarboxylic acids are selected from poly-L-lactides and poly(lactic-co-glycolic acids).

19. (PREVIOUSLY PRESENTED) The method of claim 5, wherein the phospholipids are chosen from phosphatidylglycerols, diphosphatidylglycerols containing C12 to C18 fatty acid chains, phosphatidylcholines, diphosphatidylcholines containing C12 to C18 fatty acid chains, diphosphatidylethanolamines containing C12 to C18 fatty acid chains, and diphosphatidylserines containing C12 to C18 chains.

20. (PREVIOUSLY PRESENTED) The method of claim 19, wherein the diphosphatidylglycerols containing C12 to C18 fatty acid chains are chosen from dilauroylphosphatidylglycerol (DLPG), dimyristoylphosphatidylglycerol (DMPG), dipalmitoylphosphatidylglycerol (DPPG), and distearoylphosphatidylglycerol (DSPG).

21. (PREVIOUSLY PRESENTED) The method of claim 19, wherein the diphosphatidylcholines containing C12 to C18 fatty acid chains are chosen from dilauroylphosphatidylcholine (DLPC), dimyristoylphosphatidylcholine (DMPC), dipalmitoylphosphatidylcholine (DPPC), and distearoylphosphatidylcholine (DSPC).

22. (PREVIOUSLY PRESENTED) The method of claim 19, wherein the diphosphatidylethanolamines containing C12 to C18 fatty acid chains are chosen from dilauroylphosphatidylethanolamine (DLPE), dimyristoylphosphatidylethanolamine

(DMPE), dipalmitoylphosphatidylethanolamine (DPPE), and distearoylphosphatidylethanolamine (DSPE).

23. (PREVIOUSLY PRESENTED) The method of claim 19, wherein the diphosphatidylserine containing C12 to C18 chains are chosen from dilauroylphosphatidylserine (DLPS), dimyristoylphosphatidylserine (DMPS), dipalmitoylphosphatidylserine (DPPS), and distearoylphosphatidylserine (DSPS).

24. (PREVIOUSLY PRESENTED) The method of claim 5, wherein the fatty acid esters are chosen from glycerylstearate, glyceryllaurate, cetylpalmitate, and mixtures thereof.

25. (PREVIOUSLY PRESENTED) The method of claim 6, wherein the phospholipids are chosen from phosphatidylglycerols, diphosphatidylglycerols containing C12 to C18 fatty acid chains, phosphatidylcholines, diphosphatidylcholines containing C12 to C18 fatty acid chains, diphosphatidylethanolamines containing C12 to C18 fatty acid chains, diphosphatidylserine containing C12 to C18 chains, and mixtures thereof.

26. (PREVIOUSLY PRESENTED) The method of claim 25, wherein the diphosphatidylglycerols containing C12 to C18 fatty acid chains are chosen from dilauroylphosphatidylglycerol (DLPG), dimyristoylphosphatidylglycerol (DMPG), dipalmitoylphosphatidylglycerol (DPPG), and distearoylphosphatidylglycerol (DSPG).

27. (PREVIOUSLY PRESENTED) The method of claim 25, wherein the diphosphatidylcholines containing C12 to C18 fatty acid chains are chosen from dilauroylphosphatidylcholine (DLPC), dimyristoylphosphatidylcholine (DMPC), dipalmitoylphosphatidylcholine (DPPC), and distearoylphosphatidylcholine (DSPC).

28. (PREVIOUSLY PRESENTED) The method of claim 25, wherein the diphosphatidylethanolamines containing C12 to C18 fatty acid chains are chosen from dilauroylphosphatidylethanolamine (DLPE), dimyristoylphosphatidylethanolamine (DMPE), dipalmitoylphosphatidylethanolamine (DPPE), and distearoylphosphatidylethanolamine (DSPE).

29. (PREVIOUSLY PRESENTED) The method of claim 25, wherein the diphosphatidylserine containing C12 to C18 chains are chosen from dilauroylphosphatidylserine (DLPS), dimyristoylphosphatidylserine (DMPS), dipalmitoylphosphatidylserine (DPPS), and distearoylphosphatidylserine (DSPS).

30. (PREVIOUSLY PRESENTED) The method of claim 6, wherein the fatty acid esters are chosen from glycerylstearate, glyceryllaurate, and cetylpalmitate.

31. (PREVIOUSLY PRESENTED) The method of claim 7, wherein the peptides are chosen from insulin, calcitonin, and analogues of luteinizing hormone-releasing hormone.

32. (PREVIOUSLY PRESENTED) The method of claim 7, wherein the polysaccharide is heparin.

33. (PREVIOUSLY PRESENTED) The method of claim 7, wherein the anti-asthmatic agent is chosen from budesonide, beclometasone dipropionate, and beclometasone 17-monopropionate.

34. (PREVIOUSLY PRESENTED) The method of claim 7, wherein the bronchodilator is albuterol.

35-36. (CANCELLED).

37. (CURRENTLY AMENDED) A method for administering an active principle via inhalation by the pulmonary route to a patient, comprising:

providing a biocompatible microparticle, consisting of (a) a core consisting of said active principle, and (b) an external layer of at least one coating agent for controlled release of said active principle in the patient;

wherein said external layer does not contain any of said active principle;

wherein said external layer is deposited on said core by a supercritical fluid technique;

wherein the coating agent prevents aggregation of said microparticles in a composition comprising said microparticles;

wherein said microparticles have a mean diameter of between 1 μm and ~~[[30]]~~ 15 μm and an apparent density of between 0.02 g/cm³ and 0.8 g/cm³;

wherein said active principle/coating agent mass ratio of the microparticle is between 95/5 and 80/20;

wherein an external layer comprising a residual quantity of organic solvent of less than 500 ppm when an organic solvent is added to supercritical fluid; and

wherein said microparticle is suitable for inhalation by the pulmonary route for release of the medical principle in the pulmonary tract or in alveolar region of the lungs of the patient, such that the bioavailability of the active principle in the host is at least 80% and in a therapeutic or prophylactic amount.

38-39. (CANCELLED)

40. (NEW) The method for administering an active principle via inhalation by the pulmonary route to a patient as claimed in claim 1, wherein the optional organic solvent is ethyl acetate.

41. (NEW) The method for administering an active principle via inhalation by the pulmonary route to a patient as claimed in claim 1, wherein the external layer is free of organic solvent.

42. (NEW) The method for administering an active principle via inhalation by the pulmonary route to a patient as claimed in claim 37, wherein the external layer is free of organic solvent.